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(71) Applicant (for all designated States except US): **BRISTOL-MYERS SQUIBB COMPANY** [US/US]; P.O. Box 4000, Route 206 and Province Line Road, Princeton, NJ 08543-4000 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **CARTER, Percy, H.** [US/US]; Bristol-Myers Squibb Company, Route 206 & Province Line Road, Princeton, NJ 08543 (US). **DUNCIA, John, V.** [US/US]; Route 206 & Province Line Road, Princeton, NJ 08543 (US). **MUDRYK, Boguslaw, M.** [US/US]; Bristol-Myers Squibb Company, 1 Squibb Drive, New Brunswick, NJ 08903 (US). **RANDAZZO, Michael, E.** [US/US]; Bristol-Myers Squibb Company, 1 Squibb Drive, New Brunswick, NJ 08903 (US). **XIAO, Zili** [CN/US]; Bristol-Myers Squibb Company, Route 206 & Province Line Road, Princeton, NJ 08543 (US). **YANG, Michael, G.** [US/US]; Bristol-Myers Squibb Company,

Route 206 & Province Line Road, Princeton, NJ 08543 (US). **ZHAO, Rulin** [CA/US]; Bristol-Myers Squibb Company, Route 206 & Province Line Road, Princeton, NJ 08543 (US).

(74) Agents: **DUNCAN, Laurelee, A.** et al.; Bristol-Myers Squibb Company, P.O. Box 4000, Princeton, NJ 08543-4000 (US).

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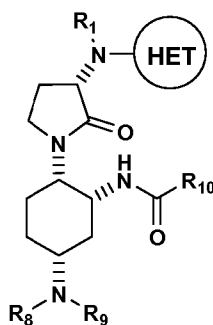
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Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

[Continued on next page]

(54) Title: MODULATORS OF CHEMOKINE RECEPTOR ACTIVITY, CRYSTALLINE FORMS AND PROCESS



(I)

(57) Abstract: The present invention provides a novel antagonist or partial agonists/antagonist of MCP-I receptor activity: N-((1R,2S,5R)-5-(*tert*-butylamino)-2-((S)-2-oxo-3-(6-(trifluoromethyl)quinazolin-4-ylamino)pyrrolidin-1-yl)cyclohexyl)acetamide, or a pharmaceutically acceptable salt, solvate or prodrug, thereof, having an unexpected combination of desirable pharmacological characteristics. Crystalline forms of the present invention are also provided. Pharmaceutical compositions containing the same and methods of using the same as agents for the treatment of inflammatory diseases, allergic, autoimmune, metabolic, cancer and/or cardiovascular diseases is also an objective of this invention. The present disclosure also provides a process for preparing compounds of Formula (I), including N-((1R,2S,5R)-5-(*tert*-butylamino)-2-((S)-2-oxo-3-(6-(trifluoromethyl)quinazolin-4-ylamino)pyrrolidin-1-yl)cyclohexyl)acetamide: wherein R¹, R⁸, R⁹, R¹⁰, and "HET" are as described herein. Compounds that are useful intermediates of the process are also provided herein.

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INTERNATIONAL SEARCH REPORT

International application No

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A. CLASSIFICATION OF SUBJECT MATTER

INV. C07D403/12 C07D207/273 A61K31/4025 C07D317/72

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

C07D A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2005/021500 A (SQUIBB BRISTOL MYERS CO [US]; CARTER PERCY H [US]; CHERNEY ROBERT J [U] 10 March 2005 (2005-03-10) cited in the application Comparative data and compounds of general formula (Ia) page 370 - page 378; tables 2A,8A-9A,12-B	1-20
X	US 2005/054627 A1 (CARTER PERCY H [US] ET AL) 10 March 2005 (2005-03-10) cited in the application claims 13-21; example 2k	1-20

☐

Further documents are listed in the continuation of Box C.

☒

See patent family annex.

* Special categories of cited documents:

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

G document member of the same patent family

Date of the actual completion of the international search

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Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040,
Fax: (+31-70) 340-3016

Authorized officer

Goss, Ilaria

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2007/074377

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-16

A compound according to claim 1, its crystalline form as well as a pharmaceutical composition comprising it and its use.

2. claims: 17-20

Process for preparing a compound of general formula VI (intermediate compound) as well as many different single compound according to claim 20 useful as intermediates in the processes described.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

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